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SENIOR THESIS

ULCERATIVE COLITIS-ETIOLOGY, DIAGNOSIS AND TREATMENT.

BRYAN T. C. FENTON

APRIL 1, 1932

ULCERATIVE COLITIS

(1) "Ulcerative colitis, may be defined as a diffuse regional or general inflammation of the colon, especially in its lower part, liable to ulceration, anatomically identical with chronic bacillary dysentery, of uncertain etiology, possessing no apparent infective properties."

The disease has been found most commonly in the second and third decade. The condition is rarely seen in the primary stage, usually having advanced to chronicity when the patient is first seen. Chronic ulcerative colitis may be and frequently is complicated by accompanying disease.

(2) "The disease was first mentioned by Wilks and Moxon, in 1875, but was first described by White, in 1888, although Hawkins believes the "pedigree of this disease can be traced back nearly three hundred years to the 'bloody flux' of Sydenheim in 1669."

"The symptomatology of chronic ulcerative colitis at the outset or during one of the exacerbations of the disease is quite characteristic. The essential clinical features of the disease are: 1. Repeated rectal discharge, varying from four to twenty stools a day, made up of soft fecal material containing blood, pus, mucus and undigested food remnants in

varying amounts, depending upon the extent and location of the ulcerative process; 2. Pain, varying in intensity from mild griping sensations to severe colicky pains, usually most marked along the course of the involved colon; 3. Fever, prostration, dehydration, loss of weight and secondary anemia. The process usually originates in the rectum and extends upward." "We may now state that the term 'chronic ulcerative colitis' has come to mean a definite disease entity which presents a characteristic clinical picture."

ETIOLOGY:

In discussing the etiology of the subject it is interesting, as well as instructive, to go back and consider the different ideas of etiology as presented by various workers.

"Hawkins, in 1909 in a consideration of the natural history of ulcerative colitis, described the hemorrhagic form with "its primary localization in the lower segment of the colon"; and emphasized the necessity of determining its exact bacteriology, not by examining the stools but by scraping the colon mucosa. He concluded that a specific serum should be ideal, since the lesions are localized and the blood is not invaded."

"Logan believes that the underlying cause of the colitis is a metabolic disturbance. Gross was able to produce minute ulcers of the colon in 3% of a large number of rats on a diet deficient in vitamins. Bassler and others believe that Bacillus

coli-communis is an important etiologic factor, asserting that this organism becomes especially virulent under proper conditions. Bassler ventures the designation of pseudodysentericus coli for the organism found predominant in some of his patients. He also says that when the organism is injected intraperitoneally into cats, rabbits or guinea-pigs, death occurs early. Many men include as etiologic factors the ordinary bacteria found in feces. Jexblake, in reports from London hospitals in 1909, considers, as factors, Bacillus coli, proteus and pyocyaneus and streptococci. White says "I have met with cases due to Bacillus coli, and some to pneumococci." Stone and Yoemans found only the usual intestinal inhabitants. Wallis found streptococci in the stool of many patients, and emphasizes the importance of mouth sepsis. Hewes speaks of idiopathic invasion of the colon in persons in perfect health. He isolated streptococci, staphylococci, colon bacilli and gas bacilli, and emphasizes the fact that often the disease appears as a sequel to another infectious disease, such as pneumonia, influenza, measles and diphtheria. Mummery considers streptococci and Bacillus coli important factors, and, in the hemorrhagic form with its spongy mucosa, the diplococcus of pneumonia as the usual cause. He says that the mucosa in this type bleeds easily, is granular, and appears as if sandpapered. Other observers believe the condition

to be the result of *Bacillus dysentericus* having disappeared from the stools and left its results with secondary invaders to keep up the infection. This would seem a plausible theory in the light of the work of Flexner and Sweet, who produced lesions from edema and small hemorrhages, and at times a diphtheritic membrane, by the intravenous injection of Shiga and Flexner dysentery bacilli or their toxins. In their rabbits, the lesions produced were primarily in the cecum and the appendix, rarely in the colon. In 1907, Morgan produced diarrhea in rats and rabbits by feeding a gram-negative bacillus, isolated from the stools of infants with summer diarrhea, differing from the ordinary dysentery bacillus in its sugar fermentation reactions. The view that the dysentery bacillus is an important factor has gained ground since the World War. Einhorn, Hurst, Leusden and others seem convinced of this theory." Bergen reports his result of two years of study regarding etiology as follows; "I was greatly impressed by the presence of large numbers of Gram-positive diplococci in smears from the lesions in the bowel of patients with ulcerative colitis and in primary cultures in glucose-brain-broth, the medium used by Rosenow, and others in localization studies. It was believed, therefore, that growth of the causative organism might occur in this medium, since it afforded a gradient of oxygen tension, whereas

only the more saprophytic organisms might develop on blood-agar plate-cultures. Furthermore, it was thought that localization in the colon might occur following the intravenous injection of the primary mixed culture, and possibly the causative organism might be isolated from the tissues of animals developing lesions."

"Working along these lines, I have been able to isolate a gram-positive diplococcus in about 90 per cent of the patients with chronic ulcerative colitis who have been examined in the clinic the last two years."

"The organism is lancet-shaped, resembling in a striking way the pneumococcus, except that it is slightly larger. In the disease producing state, it is always a diplococcus. Later after repeated subculture, it may grow in short chains so that it is probably a form of streptococcus. The strains I have tested were not agglutinated by the three types of pneumococcus serum."

(3) The Bargaen organism has found confirmation in the experience of Dr. Edmond Hogan of Washington, D. C. In all instances he was able to isolate a gram-positive that was considered to be a typical Bargaen organism. Dr. Hogan's confirmatory results are based on a series of five cases.

As yet there has not been enough time for Bargaen's work to receive extantensive checking up at the hands of other

men. Brown in this country and Seefisch in Germany, have published skeptical opinions, as experienced clinicians, of its value. Paulson, in careful studies, both by cultural methods and injection into rabbits, carried out in fourteen cases of chronic ulcerative colitis in the stage of acute exacerbation, felt that he had failed to confirm the findings or the conclusions of Bargaen. His opinion is that while streptococci of various strains are frequently found, and occasionally the Bargaen organism with all of its characteristics, the specific bacterial etiology of ulcerative colitis is still undertermined. Many writers feel that Bargaen's work is sound and should be maintained until a greater body of evidence from different workers in different clinics has accumulated.

(4) In further criticism of Bargaen's work the following is written; "The socalled Bargaen bacillus, a common denizen of the normal intestine, is not the only or even the main cause of ulcerative colitis. In ulcerative colitis (severe cases), a constitutional or local tissue cause plus the infection are the factors in its production. The infection causes are in the order of their importance clinically, but not their frequency, the two main groups of

the pyogenic streptococcus, nonhemolytic and hemolytic, one of the four parasitic types of *Bacillus coli*, a combination of one of the pyogenic streptococci and the Welsh bacillus, a combination of streptococcus and the gram-positive diplococcus of Conrad and Kurpjuweit (which the profession improperly designates as *Bargen bacillus*)."

(5) Dr. Arthur F. Hurst in reporting a series of cases which he had opportunities of sigmoidoscopy during the war calls attention to the fact, that in cases of bacillary dysentery, it is impossible to distinguish them from the ulcerative colitis with which he was already familiar.

"The author has found that not only many cases of summer diarrhoea, but many in small children diagnosed as chronic colitis, are caused by the dysentery bacillus. The organism is very difficult to isolate after the acute stage has passed, and since most cases seen are in the chronic stage it can be easily understood how rarely the organism is found. An important predisposing cause has been found in twenty-five per cent of the cases, this being achlorhydria. With this condition present, thus doing away with the normal acid antiseptic barrier of the stomach, organisms swallowed in infected water or food reach the intestines."

(6) Nesbit has set down the ulcerative condition of the colon on the following etiological bases: (1) Constitutional conditions, such as Bright's disease, gout, lead poisoning and Cardiac disease; (2) Specific bacterial or protozoal diseases, such as typhoid, pneumonia, amebic dysentery, bacillary dysentery, tuberculosis and syphilis; (3) Malignant disease; (4) Trophic disturbances due to interference with the nerve supply of the colon; (5) Mechanical trauma, such as hardened feces, foreign bodies, etc., and (6) Vascular changes, such as embolism of the mesenteric arteries and cirrhosis of the liver. Unlike Bergen and some other writers on the subject, Nesbit does not ascribe the condition to one definite etiological basis but considers it variable with stress on predisposing factors."

(7) d'Herelle in his recent work on the Bacteriophage gives no specific etiology but has carried out his work on the organism producing bacillary dysentery, with regard to ulcerative colitis. Pure cultures of this organism have been obtained by him, but because of the fact that some Bacteriophage shows a tendency to produce lysis in a variety of kindred organisms, no specificity has been mentioned with regard to a causative organism for ulcerative colitis.

Much work is being carried on at present on the subject of etiology and until the various findings of competent workers herein mentioned have either been proven or disproven the question appears as one to be classified as open.

DIAGNOSIS.

(8) "The clinical signs and symptoms of chronic ulcerative colitis include a history of frequent rectal discharges of blood, pus and mucus, mixed with feces of variable consistency, depending in a large measure on the extent to which the colon is involved. The ulceration usually begins in the rectum and spreads upward eventually to involve the entire colon. It may, however, affect any part of the colon and occasionally several parts of the colon. Early in the course of the disease, or at any time when the rectum and the recto-sigmoid only are affected, the stools may be scybalous and surrounded by or mixed with blood; there will also be frequent passages of shreds of bloody pus and mucus, with great desire to strain, and occasionally with gripping pain and tenesmus. When all or most of the colon is involved, the stools are liquid or mushy and mixed with mucus, blood and pus. Grueling cramps are not uncommon. Distress from gas, griping and various sensations along the course of

the colon are often experienced. A peculiar gray pallor is common and varying degrees of anemia exist. In the severe cases a morbid body odor prevails. An anxious, rather hopeless facial expression is not uncommon. The patients lack of bowel control with the feeling that he must remain near a lavatory may account for some of this. Much weight may be lost."

(9) The following general constitutional symptoms coupled with the stool picture above are decidedly important in making a diagnosis of the condition; "The first attack of acute ulcerative colitis or acute exacerbation of chronic ulcerative colitis is striking and characteristic. The patient is acutely ill, the fever is septic, the abdomen is diffusely tender, there may be cold perspiration, the facies is frequently anxious and severe cramps may accompany the frequent rectal discharges. Often the patient complains bitterly of soreness and tenderness of the anus." "The proctoscopic picture is pathognomonic, and an experienced proctologist does not confuse it with that of any other rectal disease. This is the stage of intense edema and hyperemia with myriads of miliary abscesses studding the mucosa, some of which have broken down to form minute ulcers."

(10) Roentgenograms and fluoroscopic examinations are aids in diagnosis and present characteristic signs. "In these studies a small, stringy, spastic colon with a feathered out or moth-eaten outline is revealed. Previous to the day of the X-ray and sigmoidoscope, accurate diagnosis of this condition was difficult or impossible. The X-ray plate and fluoroscope show spastic obliteration and partial stricture of the colon. The barium meal may be seen as a thin thread instead of the full haustrated markings. Barium enemas if given with too much force may cause enough pain and spasm to result in immediate expulsion, or, if retained, the force required to introduce the enema may be sufficient to flatten out the spastic areas and thus give a false conclusion. The barium enema is not as valuable as the meal for diagnosis of this condition."

(11) The history of ulcerative colitis aids in differentiating it from the other chronic lesions of the colon. "It is most notably a disease of long chronicity marked by a strong tendency to remissions and recurrences. While it may affect any age group, as a case has been reported in a child of three years and the writer has had a patient of sixty-six, yet in most instances young adults are the victims. The age incidence and the prolonged and intermittent course are usually

quite sufficient to exclude malignant disease. The same factors might not so definitely point against the tuberculosis or lues, and certainly do not exclude amebic colitis, which has much the same clinical course. Here the aid of special examinations must be invoked. The microscopic search for specific organisms in the stool is an essential step in reaching a diagnosis, but even the failure to discover such organisms is not conclusive, as the difficulty in finding amebae and tubercle bacilli at times is well known." The proctoscope or sigmoidoscope is of the greatest value, and no examination of a patient with a continuing bowel disorder is complete without the use of such an instrument. The use of such instruments and the pictures resulting has been discussed.

TREATMENT.

(11) "Under the heading of general medical care come rest in bed, a diet that is rich in calories but free from vegetable or other irritating residue, the supplying of abundant fluids to the tissues, the use of sedatives for pain and diarrhea, the administration of bismuth or other soothing and coating substances by mouth, the use of blood transfusion as indicated and stimulants for failing circulation."

"Local treatment for the bowel fall into three

classes; irrigations, insufflations, and topical applications. The variety of solutions that have been employed is very great. Tannic acid, silver preparations, and permanganate of potash are among the drugs frequently employed, all being used in weak dilutions to start with. These irrigations must be run in slowly, without too much pressure behind them. Insufflation with various powders has had a certain popularity but because of the limited area of the bowel reached and because of some fatal accidents due to rupture of the diseased gut from too great a pressure or to sudden an expansion by air pressure, this has been largely discarded."

Topical applications direct to the lesions through the sigmoidoscope is another method of obviously limited scope and of doubtful value. No specific treatment has as yet won any wide recognition.

(12) The work of Bergen relative to vaccine therapy has received much recognition and results both pro and con have been reported by those adopting this type of treatment.

Bergen in reporting his findings from the use of the vaccine suggests the following treatment. "(1) Immunization, vaccination or desensitization against the predominant bacterium found in these cases. (2) Removal of all distant foci of infection. (3) Generous, liberal, high caloric diet."

1. "This is accomplished by administration to patients

who are less severely ill, of vaccines prepared from the diplostreptococcus, isolated from the rectal lesions of patients with the disease and, to the patients who are more severely ill, a specific antibody solution (concentrated serum) prepared by immunization of horses."

2. "All demonstrable foci of infection should be eradicated as far as possible. Teeth with periapical abscesses, infected tonsils, and even tonsils that are suspected of being infected should be removed. Prostatic infection is difficult to treat in these cases and probably should not be tampered with."

3. "What the patient should eat varies with the severity of the disease. Little digestion takes place in the large intestine, and unquestionably too much dietary limitation has been practiced in the past. Diet for the ambulatory patients as employed at the Mayo Clinic, consists of 3000 calories of food of high caloric value and low residue. Attention is paid to an adequately balanced ratio of vitamins. This diet will be varied in accordance with the activity of the disease. At times it has to be initiated by the administration of liquids only, but even these should be high in calories. Many of the patients tolerate milk poorly. Therefore, this is added to the diet only when patients, who have

previously limited their diet, often to extreme degrees, begin to relish their food."

"Administration of glucose intravenously and of solutions of sodium chlorid subcutaneously occasionally become necessary in more severe, fulminating cases. Sedatives in the form of camphorated tincture of opium and codeine are helpful in cases in which there is much pain, tenesmus and frequent stools. The powders, such as bismuth, tribasic calcium phosphate and kaolin, are temporarily helpful. Hot abdominal stupes become necessary in rare instances. There are a number of drugs, the administration of which gives symptomatic improvement in selected cases. Among these the most helpful have been iodine, gentian violet and arsenic. Because of the ever present danger of symptoms of arsenic poisoning, arsenic is to be held in reserve as a drug to try when other measures fail."

(13) Fradkin and Gray in reporting a series of fifteen cases give the following with relation to the preparation of vaccine as done by Barga, and the therapy with the same:

"Material for the culture was obtained by inserting a long sterile swab through the sigmoidoscope and scraping the depths of an ulcer. This material was transferred to warm dextrose broth and incubated for six hours. The short incubation period is an important part of the technique, as otherwise the colon

group of organisms outgrow and destroy the diplococci. Smears are made and stained by Gram's method. If the typical gram-positive organisms described by Barger are present, subcultures are grown in other dextrose broth tubes for twelve hours. If the organisms are still present in these culture tubes as determined by direct smear, litmus lactose and blood agar plates are inoculated with material from the last culture tubes. Within from eighteen to twenty-four hours the characteristic small, round, slightly raised, grayish, dry colonies are fished out. The strain of the organism is preserved by making subcultures every forty-eight hours. After the completion of the fermentation tests and bile solubility tests, vaccines are made by growing the organisms on dextrose agar slants. The vaccine is so standardized as to contain approximately two billion organisms per cubic centimeter."

"The autogenous vaccine was administered subcutaneously to each of twelve patients three times a week for a period of eight weeks. After eight injections, improvement was noted in ten patients. The tenesmus was relieved, the number of stools decreased rapidly from as high as fourteen a day down to three, and a gain in weight was noted in each case. The hemoglobin and erythrocyte count increased in a short

period. After eight weeks the patients reported that they felt better than ever before during their illness. In two patients vaccine therapy had to be continued for four months before the disease could be checked and all symptoms relieved. Relapses were reported in 3 cases, and another course of vaccine therapy was instituted, this time bringing lasting results."

(14) Bassler reports some degree of success with the following treatment, this being especially valuable in the prevention of remissions; "A small enema, provided for immediate ejection is used. This type of irrigation is carried on with any one of these solutions, permanganate of potassium from 1:10,000 to 1:1000; warm mercurochrome 1:5000 to 1:1500; neutral acriflavine 1:10,000 to 1:500; ichthyol, fluid from 4.0 to 1.000. Using the small enema the following advantages were found:

1. The inflow of water, with the irrigating bag about two feet up, is a small stream so that the much larger outlet space immediately returns it. In this way the accumulation of fluid possible of being retained in the bowel does not reach higher than the dome of the rectum and does not accumulate and reach high in the colon as does an enema or the usual recurrent rectal tube. (This is important in that one must be careful not to carry the infection upward).

2. It is easily retained and comfortable during use in either the lateral or sitting position of the patient.

3. It is sterilizable without destruction as is the case with hard or soft rubber tubes."

"Night treatment has been found to be an important consideration and is carried on as follows: Instillations of four ounces of the following suspension as recommended by Dr. Landsman: Iodoform 8.0, Bismuth subnitrate 120.0, Olive oil 1000.0. This is to be retained. Secondly, the coating of the gut, every other day, through the proctoscope with a half and half mixture of calomel and bismuth subnitrate powder to which iodoform or some other antiseptic in powder form may be added. The purpose of this treatment is to, as far as possible keep the condition localized to the rectum and lower colon, this being feasible because of the accessibility of this portion of the bowel. The author is of the opinion that even though a cecostomy has been performed and daily injections employed, the lower canal should be treated from below."

(15) With a view of determining the value of Ionization as a treatment for colitis, Burnford reviewed a consecutive series of 28 cases so treated. In some, ionization was the sole treatment, in others, it was tried after various other methods had failed. There were 21 cures. Six patients re-

lapsed, and four were again treated with satisfactory results; the other two did not carry out the instructions and failed to get relief. Two failures are still alive, but one of these ascribed the improvement in his general health and increase in weight to ionization. Included in the series are three fatal acute cases which ran a rapid course, and some chronic cases which were apparently incurable.

"A special flushing electrode was used. The ionization is carried out while the zinc solution is passing in. At first a two per-cent solution was used but later only one-half per-cent in quantity up to the limit of tolerance. At first only a little may be tolerated with 2 or 3 Ma. of current, but finally three pints may be held whilst a current of 20 Ma. is passing for fifteen minutes or longer. In all cases the dietetic factor was viewed as important and hence a liberal light diet was always allowed."

"Cure was judged by the presence of normal stools containing no pus, and to a lesser degree as only a part of the bowel falls within the field of vision--sigmoidoscopic evidence."

(16) Edmond Nelson has applied the D'Herelle phenomenon or bacteriophage as a means of treatment. "Cultures were made from the ulcerations of each patient. The swabs taken were

planted on blood agar and litmus lactose agar plates. A considerable amount of contamination would be expected, but it was found that after twelve hours incubation, four of the plates contained pure cultures of *Bacillus pyocyaneus*. The other four plates contained mixed cultures of *Bacillus coli*, *Bacillus proteus*, *Bacillus sporogenes*, and *streptococcus haemolyticus*."

"In making a bacteriophage from the mixed cultures it was thought best to use them in mixed cultures and not to isolate them into their various groups."

"The bacteriophage was prepared by taking samples of water from the Mississippi river near the entrance of a sewer, as this would aid in securing as many intestinal organisms as possible. Ten cc. of this water was added to five-hundred cc. of beef broth bouillon, and incubated for a period of thirty-six hours. One cc. of this material was then added to ten cc. of a beef broth culture of the organisms obtained from the ulcerations of each individual patient. This method had to be repeated numerous times with many samples of the river water before a bacteriophage was obtained for each culture. After repeated incubations this bacteriophage would cause a lysis of 10 cc. of the beef broth culture in about fifteen minutes. Large quantities of the bacteriophage could now be made very readily by adding one or two drops to a flask of 1,000 cc. of

beef broth and incubating it for twelve hours."

"Each patient was given two liters of the bacteriophage daily by mouth. It was made more palatable by adding flavoring and fruit juices. One liter was given daily by Murphy drip, one half cc. was given subcutaneously daily, and one liter was used in the form of an enema. The four patients from whom pure cultures of *Bacillus pyocyaneus* had been obtained showed marked improvement after three days of treatment. After three weeks treatment there was a considerable decrease in the size of the ulcerations, and in six weeks there were no clinical symptoms and no evidence of ulceration."

"The group that apparently had mixed infection in the ulcerated area did not seem to respond to this type of treatment nearly as well. In two of the patients there was considerable improvement after two weeks treatment and also some decrease in the size of the ulceration. The two remaining cases in this group did not receive much relief from this treatment and became quite nauseated from taking the bacteriophage by mouth. This treatment was discontinued and the patients again placed on a low residue diet with local applications to the ulcerated area."

(17) Haskell and Cantarow have reported an experimental and a clinical study of the non-specific form of ulcerative

colitis. The work covers a series of seven cases of ulcerative colitis in which the diffusibility of calcium was determined. Simultaneous determinations of the calcium content of the blood serum and cerebrospinal fluid were made in the seven cases.

"The serum calcium ranged from 8.71 to 11.25 mg. per 100 cc., the diffused calcium from 4.25 to 6.15 mg. and the non-diffused calcium from 2.56 to 6 mg. The ratio of diffused to non-diffused calcium varied between 83 and 240 per-cent."

"In a previous investigation, the normal partition of calcium was found as follows: Serum calcium 9 to 11 mg., diffusible calcium 4.5 to 5.5 mg. and non-diffusible calcium 4.7 to 5.75 mg. per 100 cc., the ratio of the diffusible to the non-diffusible fraction being 82 to 115 per-cent. In a subsequent study it was noted that in practically all patients with some manifestation of allergy or autonomic imbalance, the diffusibility of calcium was increased. This was evidenced by an increase in the ratio of diffused to non-diffused calcium."

"The rationale of calcium and parathyroid therapy in ulcerative colitis rests upon the beneficial effect of calcium on the following existing conditions: (a) Nutritional change in the tissues, with or without a disturbance of calcium partition; (b) spasticity of the colon; (c) haemorrhage."

"The form of treatment includes: (1) a cellulose-free,

non-irritating diet; (2) belladonna and kaolin; (3) calcium salts, ammonium chloride and parathyroid extract administered as follows:

Calcium chloride, calcium lactate and calcium gluconate were the salts used. The gluconate was found to be more easily tolerated. It must be remembered that calcium is absorbed best when the intestinal alkalinity is lowest. Therefore to secure maximum absorption, it must be administered at times when upper intestinal digestive activity is at a minimum, that is, a short time before meals. Calcium gluconate, 60 gr. was, therefore, administered orally three or four times daily, three and a half to four hours after meals."

"Ammonium chloride by increasing the hydrogen-ion concentration of the tissues causes an increase in the availability or utilization of the tissue calcium. Ammonium chloride is well tolerated by the majority of patients. It is administered in doses of 20 to 30 gr. in capsule or powder form, together with the calcium salt."

"Collip states that the function of the parathyroid hormone, in the normal animal, appears to be that of a regulator of calcium metabolism, and its action is primarily as a calcium mobilizer. Our investigations into the action of parathyroid extract suggest that its injection results in an increase in the availability and utilization of calcium, as well as in a

tendency toward the restoration of a normal ratio of diffusible to non-diffusible calcium."

"Parathyroid extract (Para-thor-mone) is injected intramuscularly, the average adult dose being 20 to 30 units, varying with body weight. The injections are repeated at intervals of forty-eight to seventy-two hours, depending upon the severity of the symptoms."

"Of the 13 patients, only ten have been observed over a sufficient period of time to permit of definite conclusions. Of the remaining 3, 2 improved symptomatically to a degree which led them to discontinue further treatment. It is therefore, in a group of 10 patients that the effects of calcium and parathyroid are reviewed. In 8 patients the mucous membrane of the lower bowel returned to a practically normal state after all symptoms subsided and has remained so."

"In all patients cessation of bleeding was the earliest and most constant feature. Whether healing of an ulcer preceeds or follows the interruption of bleeding is a controversial point. However sigmoidoscopic examination has repeatedly disclosed unhealed ulcers without evidence of bleeding. The influence of calcium and parathyroid upon hemorrhage is regarded as an important factor in accounting for their beneficial effect upon the lesions of ulcerative colitis."

"The pain produced by spasm, as well as its inhibitory effect upon healing, are recognized, and an attempt is always made to reduce this excessive muscle tonus. Belladonna was used to the limit of tolerance with little relief, but on changing to calcium and parathyroid a marked relaxant effect was noted."

(18) "Nesbit has mentioned as an adjunct to vaccines and local treatment, the administration of the standard tincture of iodine, ten drops in a glass of water immediately after each meal. This was used because the combination of iodine administration and the vaccine caused a more rapid disappearance of the streptococcus from the stools and a more rapid healing of the ulceration."

(19) Arn in writing relative to surgical treatment of colitis emphasizes the fact, that all cases of chronic ulcerative colitis should be subjected to thorough medical treatment before any surgical procedure upon the colon is contemplated.

Arn describes a surgical procedure which was successful in five cases of chronic ulcerative colitis refractory to the usual forms of medical treatment.

"The abdomen is explored through a long left pararectus incision, the lower end of the incision ending about one inch above the spine of the pubic bone. Careful exploration is made of all abdominal viscera for active foci of infection, which are

removed if the condition of the patient justifies the procedure. The colon is then explored with as little handling as possible in order to prevent any recurrence of bleeding. If the previous proctoscopic examination has revealed only a grade 1 or grade 2 ulceration of the rectum and if the caliber of the sigmoid colon near its junction with the rectum is sufficiently large, and the bowel is freely movable, a lateral anastomosis is made between the terminal ileum and the sigmoid colon. The ileum is prepared for anastomosis by clamping it with two crushing forceps eight inches from the cecum and inverting the ends with two purse-string sutures of silk. The distal end of the ileum is brought through a stab opening at McBurney's point and is attached to the skin for future irrigations. It is not opened however for 72 hours, in order that the peritoneum may become sealed about the opening."

The postoperative care is primarily that of any abdominal operation. Irrigations of the large bowel are begun at the end of two weeks. During the period of hospitalization, a solution of 1:5000 acriflavin is used. A catheter is inserted into the enterostomy opening and a rectal tube is placed in the rectum. Two liters or more of the acriflavin solution are required for each irrigation. The patient is taught to irrigate

the colon before leaving the hospital, and ultimately the rectal tube is omitted, the patient being instructed to sit on a commode or toilet seat. Normal saline solution is substituted for acriflavin after the patient leaves the hospital. The patient is urged to carry out the irrigations once each day for an indefinite period."

"The enterostomy opening is not closed. There is very little discharge; a small piece of gauze will usually suffice as a daily dressing."

"The improvement is ordinarily quite rapid, the irrigations usually being free from mucus and blood by the end of the fourth week."

(20) Barger in writing of ulcerative colitis, stresses the value of mental hygiene, and declares that it cannot be overemphasized. He further states; "A physician caring for these 'toilet stricken' patients spends much time encouraging them. Rest in bed should be abandoned early. Fresh air, sunshine and mental diversions are valuable assets in the treatment. It is important to encourage the patient to eat; frequent weighings has its purpose."

Treatment of ulcerative colitis may be summed up under five general headings; 1. General Medical care; 2. Vaccine treatment; 3. Drug therapy; 4. Surgical treatment; 5. Mental hygiene.

With the variation of symptoms presented, symptomatic treatment seems to be the most logical form of therapy. Various writers in their enthusiasm, have in the past overemphasized the value of certain drugs and procedures, no doubt in good faith. At present much work is being carried on in this country and in Germany, with regard to bacteriophage treatment, and from reports of competent workers, it holds promise not only in ulcerative colitis, but in many cases where an organism has been determined as the etiological basis of the condition. Since a definite etiological basis is lacking for ulcerative colitis, this would seem to me to be the outstanding factor necessary to be determined before a true scientific treatment is instituted.

Bargen's vaccine treatment has received praise and condemnation at the hands of the profession, but no doubt it is as worthy of trial in this condition as other non-specific treatments now in vogue.

Surgery has met with some degree of success, but to the average patient and practitioner at present it seems to be held more as a measure of last resort, and surgery as a last resort is frequently carried out at a time when the patient is in poor condition for such radical treatment. Should true value of this procedure be determined, it would seem wise to carry it out earlier in the disease when the patient's resistance

is such that a favorable outcome may be anticipated.

With regard to mental hygiene, there can be no dispute as to its value no matter what the diseased condition may be. In a disease with the chronic aspect, such as is presented in ulcerative colitis, mental hygiene might well be classified as one of the true, definite points of treatment now known to be of value.

The treatment as now carried out must necessarily be classed as that of trial and error, and while good results are reported, no definite scientific treatment has as yet been found.

Case Reports

Case 1.

Patient #43463, University of Nebraska dispensary. Age 27 years, female, white. (1-26-29)

Complaints on entering dispensary:

1. Hemorrhoids past six months, with bleeding and itching.
Prolapse of hemorrhoids during and following bowel movement.
2. Marked flatus at any time of the day following ingestion of any type of food.
3. Low lumbar backache, when on feet.
4. Bowels loose, three to four movements per day.
5. Blood and mucous in the stools.
6. Loss of weight and weakness.
7. Tenderness in region of epigastrium

Operations:

Hemorrhoidectomy two years ago.

Family History:

Cancer of the liver in Maternal grandmother.

Physical Examination:

Tenderness and slight rigidity over McBerney's point.

Tenderness in region of epigastrium.

Laboratory:

Urine negative, cervical smears negative, Wasserman negative.

Brain broth culture from rectum;

1. Gram neg. bacilli, few gram positive bacilli in chains.
No Bargen's bacilli, transparent B. coli.
2. Gram neg. bacilli, few streptococci, no Bargen's bacilli,
B. coli.
3. Gram neg. bacilli, organisms suggestive of Bargen's
bacilli.

Treatment:

B. and B. capsules, Milk of bismuth, soft bland diet.

Follow up and subsequent treatment:

Hospitalization (11-23-31)

Hospital treatment;

1. Antigen given
2. Bacteriophage insillations - resulting in cramping
and frequent stools, discontinued.
3. Proctoscopic - application of silver-nitrate to
ulcerated areas.
4. Opium suppositories.

Results - On leaving hospital 1 bowel movement per day
for a week.

Dispensary (12-29-31) Patient reported for check up, procto-
scopic showing considerable edema and inflammation with ulcer-
ation. Suggestion of beginning acute exacerbation. Sent to
county hospital for one month treatment, and outcome there not
obtainable.

Case 2.

Patient #50756, University of Nebraska dispensary. Age 28 yrs., male, white. (3-2-31)

Complaints on entering dispensary:

1. Sharp pain in region of epigastrium about 8 months ago.
This pain has no relation to meals.
2. Water diarrhea.
3. Three to eight bowel movements per day.
4. Patient must remain in vicinity of toilet as desire to defecate comes on quickly.
5. After defecation pain is relieved.
6. Blood and mucous in the stools.
7. Flatus quite marked.

Operations or previous illness:

1. Swelling of ankles at night.
2. Chronic cough past two years.

Family History:

Negative

Physical Examination:

Slight tenderness and rigidity of left lower quadrant.
Rectal examination - shows sphincter quite tight and tender.
Proctoscopic examination - shows a condition of hypertrophic proctitis, large fissure on posterior aspect of the anal canal, evidence of hemorrhoids, slight ulceration of lower colon.

Laboratory:

Urine negative. No stool examination recorded.

Treatment:

Fissure treated.

Bismuth subnitrate grains 10, calcium carbonate grains 10, q.i.d.

Colon irrigation, soft diet, Kaomin by mouth.

Follow up and subsequent treatment:

3-30-31. Patient reported at dispensary. Ulcerations improved, 2 - 3 bowel movements per day. Continue same treatment.

4-14-31. Patient reported at dispensary. Slight improvement in condition of rectal mucosa as compared with 1 month ago. There is still considerable pitting and proliferation, mucosa bleeds easily, numerous small, granulating ulcers present.

Treatment - Acroflavine 1:500 solution ounces eight. Dilute 1/2 ounce with 2 glasses of water and irrigate daily.

Case 3.

Patient #52351, University of Nebraska dispensary. Age 34 years, female, white (8-3-31)

Complaints on entering dispensary:

1. Caseous, mucous discharge with bowel movement with small amount of blood.
2. Condition began 2 years ago, and at that time discharge was in morning only, but now may be at any time.

3. Slight tenderness over epigastrium, relieved by bowel movement.
4. Constipation and diarrhea alternating.
5. Slight loss of weight.

Operations and previous illness:

Heart trouble for a number of years.

Family History:

Negative.

Physical Examination:

Presystolic murmur over Erb's point.

Rectal and proctoscopic examination - shows low grade proctitis, atrophic in type, wall smooth, slightly injected, some pus mixed with feces.

Laboratory:

Stools suggestive of amoeba.

Eggs of amoeba found in stool.

Treatment:

Yatrin instillations, ounces six, 1% once daily.

Follow up and subsequent treatment:

9-22-31. No signs of blood or pus in stool and only a small amount of mucous present.

11-7-31. Blood in stool each morning. Proctoscopic examination shows small ulcers in lower colon. Small amount of blood

and pus seen.

Treatment - Yatrin tablets #40, two tablets, t.i.d., p.c.

Yatrin solution 15%, 8 ounces. Use 1/2 ounce in glass of water for rectal instillation.

Case 4.

Patient, M. S. Outcall service, U. Of N. dispensary. Age 7 years, female, white (10-8-31)

Complaints when seen on outcall:

1. Diarrhea past two days.
2. Slight nausea and temperature of 100 degrees for past two days.
3. Blood and mucous in stool.
4. Watering of eyes.
5. Sore throat.
6. Generalized slight abdominal pain and tenderness.

Operations or previous illness:

Subject to upper respiratory infections each winter, measles, whooping cough, tonsillitis.

Family History:

Mother and one other young child have had practically the same condition in the past month.

Physical Examination:

Tenderness along the course of the colon and slight rigidity.

Body warm and moist.

Tonsils large and injected.

Treatment:

B. and B. Capsules. Prescription as follows: aspirin 10 grs., phenacetin 5 grs., simple syrup q. s., ad. ounces 2.

Non-residue diet, cold sponge bath, normal saline enema.

Follow up and subsequent treatment:

10-10-31. Temperature 99.5. Blood still present in stool.

10-15-31. Temperature normal, stools loose, but no blood.

Patient feeling much better.

Case 5.

Patient #33837, University of Nebraska dispensary, Age 52 years, female, white.

Complaints on entering the dispensary:

1. Constipation and diarrhea alternating.
2. Bad taste in the mouth.
3. 8 - 10 bowel movements per day.
4. Occasional blood and mucous in the stools.

Operations or previous illness:

Stomach trouble for a long period of time.

Family History:

Negative.

Physical examination:

Submaxillary glands bilaterally enlarged.

Tonsils congested.

Tenderness in region of umbilicus, left iliac region and at Murphy's point.

Proctoscopic examination - Mucous membrane shows a few small ulcerations and slight discharge, membrane slightly injected.

Treatment:

Yatrin solution 4%.

Potassium permanganate solution for irrigations, yeast q.i.d., Kaomin, cod liver oil.

Laboratory:

Wasserman negative, urinalysis negative.

Follow up and subsequent treatment:

After 1 months treatment bowel movements came down to 2 per day, all well formed and only a slight amount of mucous. Feeling much better.

2 months later - Hospitalization.

Diagnosis of Pellagra and ulcerative colitis. Pain in the abdomen - generalized for 3 weeks time. Thought to be an acute abdomen on entering hospital. Yatrin treatment in hospital.

Case 6.

Patient #54379, University of Nebraska dispensary, Age 40 years, male, white.

Complaints on entering dispensary:

1. Generalized weakness.
2. Blood in stool since two years ago becoming progressively worse.
3. Loss of weight - about 45 pounds in 2 years.
4. Gums bleed easily.
5. Constant thirst.
6. Relieved by a bloody, watery stool.
7. Stools are sometimes bright red, and sometimes contain blood clots.

Operations or previous illness:

Typhoid fever at 11 years of age, very severe. Diabetes at present.

Physical examination:

Pyorrhea. Tonsils congested and enlarged. Cervical glands readily palpable.

Abdomen - tenderness over McBerney's point and at umbilicus.

Proctoscopic examination - shows polyposis of colon. Hemorrhoids present. Some slight ulceration of the colon.

Laboratory:

Wasserman negative, blood count W.B.C. 8,200, R.B.C. 5,500,000, Hemoglobin 104%. Urine, S.G. 1,032, Sugar 2 plus, Blood sugar 237-280 mgs.%.

Xray - Barium enema showed a few indefinite filling defects in the descending colon, multiple polyposis of the colon.

Discussion of cases presented:

In the series of six cases presented the following constant findings are worthy of mention;

1. The age range is chiefly in the second and third decade.
2. The history of foci of infection is fairly constant.
3. Diarrhea and constipation alternating.
4. Blood and mucous present in the stools.
5. Pain in region of epigastrium.
6. Temperature slightly abnormal.
7. Weakness and loss of weight.
8. Increased number of stools per day.
9. Proctoscopic examination reveals ulcerations.
10. Tendency to recurrence.

The cases as given were seen in part in the University of Nebraska College of Medicine dispensary, and in part on the outcall service of the dispensary. The cases could not be followed up as carefully or as long as might be desired, and three of the six cases are at present receiving treatment in the G. I. clinic at the dispensary.

Hospitalization seems to be advisable at times, but does not seem to reduce the factor of recurrence. In some of these patients, it is a known fact that cooperation is lacking, and therapy as prescribed is not carried out after leaving the hospital.

In the series of cases a variation in treatment has been carried out with variable results. In most cases the ulcerations improved under treatment and the number of stools per day were reduced. With a cessation of symptoms the patients as a rule discontinued treatment and were not again seen until an acute exacerbation called for attention and brought them to the dispensary.

In these patients, especially the younger individuals, the mental attitude was none to good, since being "Toilet Stricken" (as Bergen expresses it) the natural social activities were necessarily curtailed. With a relief of the frequent stools came a change in mental attitude, and on this basis, if no other, better cooperation with subsequent regular checkup is usually obtained in individuals in the second decade of life, thus allowing a better evaluation of methods of treatment and tendency to recurrence.

The drug yatrin, orally and in irrigations gave probably the best results in dispensary practice. In conjunction with this, regular proctoscopic examination and painting of ulcerations with 20% silver nitrate served to keep down the irritation and give a relief of symptoms.

Summary:

1. Etiology;

Ulcerative colitis is conceded by most writers to be infectious.

Suggested causative organisms.

- (a) Bargen's bacillus
- (b) Bacillary dysentery
- (c) Bacillus coli communis.
- (d) Streptococci
- (e) Proteus
- (f) Pyocyaneus.
- (g) Pseudodysentericus coli
- (h) Diplococcus of pneumonia.

Sequelae to other infections and infectious diseases.

- (a) Mouth sepsis
- (b) Appendicitis
- (c) Pneumonia
- (d) Influenza
- (e) Measles
- (f) Diphtheria.

2. Diagnosis;

(a) Proctoscopic and sigmoidoscopic examination by the characteristic picture.

(b) Rectal discharge of blood and mucous mixed with feces.

- (c) Pain and tenesmus.
- (d) Varying degrees of anemia.
- (e) Disturbed mental attitude.
- (f) Weight loss.
- (g) Roentgenologic study characteristic of the condition. Fluoroscopic examination valuable.
- (h) Septic temperature in the acute attack.
- (i) History of remissions and recurrences in the chronic state.
- (j) Microscopic and gross stool examination for specific organisms.

3. Treatment;

- (a) Erradication of foci of infection.
- (b) Supportive treatment.
- (c) Diet.
- (d) Vaccine therapy (Bargen)
- (e) Local medication.
- (f) Drugs orally and by irrigation.
- (g) Bacteriophage.
- (h) Surgery, as indicated.

Conclusions:

1. Etiology - questionable, but probably on an infectious basis.
2. Diagnosis - best by proctoscope, sigmoidoscope, Xray and

fluoroscope, together with history.

3. Treatment - best by removal of foci of infection and by local application, irrigation and oral medication. Surgery of value as a life saving measure.

4. Prognosis - Good^{???}, as long as treatments are continued, but prone to recurrence regardless of treatment.

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